

Dean Engelhardt et al.  
Serial No.: Not Yet Assigned  
Filed: Herewith  
Page 2 (Preliminary Amendment Accompanying Request for a  
Continuation Application Under 37 C.F.R. §1.60 - April 9, 1993)

-- CROSS-REFERENCE TO OTHER RELATED APPLICATIONS

This application is a continuation of U.S. Application Serial No. 07/532,461, filed on May 31, 1990, which is a division of U.S. Application Serial No. 07/140,980, filed on January 1, 1988, abandoned, which is a continuation of U.S. Application Serial No. 06/674,352, filed on November 21, 1984, abandoned, which in turn was a continuation of U.S. Application Serial No. 06/391,440, filed on June 23, 1982, abandoned.--

Page 2, line 1, change "quantatively" to --quantitatively--.

Page 2, line 20, between "April 17, 1981." and "The disclosures of this" insert the following sentence:

--Serial No. 255,223 was abandoned in favor of continuation application, U.S. Application Serial No. 496,915, filed on May 23, 1983, now U.S. Patent No. 4,711,955. Therefore, the disclosure of U.S. Patent No. 4,711,955 is herein incorporated by reference and made part of the instant disclosure.--

Page 3, sixth line from the bottom of the page, change "emcompassed" to --encompassed--.

Delete the following portion of the specification:

Page 4, line 1, through page 52, line 18.

Page 52, lines 20 and 21, change "The aforementioned publications are herein incorporated and made part of this disclosure" to read as follows:

--The publications cited in the aforementioned U.S. Patent No. 4,711,955 are also herein incorporated and made part of this disclosure.--

Page 90, 7th line from the bottom of the page, after "P moiety" and before the comma ",",

insert --(also designated hereinbelow as "PM")--.

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Page 90, 6th line from the bottom, after the first word in the line  
"moiety" and before the comma ",", insert  
--(also designated hereinbelow as "SM")--.

Page 90, 6th line from the bottom, after "a base B moiety" and  
before the comma ",", insert  
--(also designated hereinbelow as "BASE")--.

Page 90, 4th line from the bottom, after "P, S or B moiety" and  
before the comma ",", insert  
--(referred to hereinbelow as "PM," "SM"  
and "BASE," respectively)--.

Page 90, 3rd line from the bottom, after "various base B moieties"  
insert --(BASE)--.

Page 93, line 3, after "B moieties" and before the comma ",",  
insert --(PM, SM and BASE, respectively)--.

Page 93, line 4, after "and/or B moieties" and before the period "."  
insert --(PM, SM and BASE, respectively)--.

Page 93, line 9, before the first word of the line "wherein"  
insert --(PM — SM — BASE — Sig)--.

Page 93, line 9, after "P" insert --(PM)--.

Page 93, line 10, after "S" insert --(SM)--.

Page 93, line 11, after "the base moiety" insert --(BASE)--.

Page 93, line 12, after "P" and before "is attached" insert --(PM)--.

Page 93, line 13, after "S moiety" insert --(SM)--.

Page 93, line 15, after "base B moiety" insert --(BASE)--.

Page 93, line 17, after "S moiety" insert --(SM)--.

Page 93, line 19, after "B moiety" insert --(BASE)--.

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Page 93, line 23, after "P - S - B - Sig"  
 insert --(PM — SM — BASE — Sig)--.

Page 93, last line, after

$$\begin{array}{c} \text{"Sig"} \\ | \\ \text{P} - \text{S} - \text{B} \end{array}$$

insert

$$\begin{array}{c} - - \text{ (Sig} \\ | \\ \text{PM} - \text{SM} - \text{BASE)} \end{array} \quad - - .$$

Page 94, line 3, after "phosphoric acid moiety" insert --(PM)--.

Page 94, line 4, after "sugar S moiety" insert --(SM)--.

Page 94, line 5, after "base B" insert --(BASE)--.

Page 94, line 6, after "sugar S moiety" insert --(SM)--.

Page 94, line 6, after "base" insert --(BASE)--.

Page 94, line 8, after "sugar S moiety" insert --(SM)--.

Page 94, line 9, after "S moiety" insert --(SM)--.

Page 94, line 17, after "P - S - B" insert the following

$$\begin{array}{c} - - \text{ Sig} \\ | \\ \text{PM} - \text{SM} - \text{BASE} \end{array} \quad - - .$$

Page 94, line 19, after "moiety," insert --(SM)--, both occurrences.

Page 94, line 26, before the first word in the line "wherein" insert the following:

$$\begin{array}{c} - - \text{ Sig} \\ | \\ \text{PM} - \text{SM} - \text{BASE} \end{array} \quad - - .$$

Page 94, line 26, after "P" insert --(PM)--.

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Page 94, line 27, after the first word in the line "moiety"  
insert --(SM)--.

Page 94, line 27, after "B" insert --(BASE)--.

Page 94, line 28, after "the P moiety" insert --(PM)--.

Page 94, line 29, after "the S moiety" insert --SM--.

Page 94, line 31, after "The base B" insert --(B)--.

Page 94, line 32, after "the B moiety" insert --(BASE)--.

Page 95, line 1, after "said B moiety" insert --(BASE)--.

Page 95, line 4, after "moiety" insert --(PM)--.

Page 95, line 10, after "P moiety" insert --(PM)--.

Page 95, line 19, after "P - S - B - Sig" and before the comma ",",  
insert --(PM — SM — BASE — Sig)--.

Page 95, line 21, after "moiety" and before "at" insert --(BASE)--.

Page 95, line 22, after "moiety" and before "is" insert --(BASE)--.

Page 95, line 23, after "the B moiety" insert --(BASE)--.

Page 96, line 5, after "acid moiety P" insert --(PM)--.

Page 96, line 5, after "sugar moiety S" insert --(SM)--.

Page 96, line 5, after "base moiety B" insert --(BASE)--.

Page 96, line 6, after "P-S-B" insert --(PM — SM — BASE)--.

Page 96, line 11, after "the P moiety" insert --(PM)--.

Page 96, line 11, after "the S moiety" insert --(SM)--.

Page 96, line 12, after "the B moiety" insert --(BASE)--.

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Page 96, line 13, after "P-S-B" insert --(PM — SM — BASE)--.

Page 96, line 15, after "P-S-B" insert --(PM — SM — BASE)--.

Page 96, fourth line from the bottom of the page,  
change "peroxidase or" to --peroxidase, --.

Page 96, third line from the bottom of the page,  
change "nuclease." to --nuclease, acid phosphatase or  
β-galactosidase.--

Page 97, 10th line from the bottom of the page, after "base B  
component" and before "therein" insert --(BASE)--.

Page 97, 9th line from the bottom, after "the sugar S component" and  
before "therein" insert --(SM)--.

Page 97, 8th line from the bottom, after "component" and before  
"thereof." insert --(PM)--.

Page 97, last line, after "255,223" and before the period "." insert  
--, now U.S. Patent No. 4,711,955 --

Page 98, line 7, after "S or B moieties"  
insert --(PM, SM or BASE, respectively)--.

Page 103, line 13, after "P" insert --(PM)--.

Page 103, line 13, after "S" insert --(SM)--.

Page 103, line 14, after "B" insert --(BASE)--.

Page 103, line 16, after "P, S or B moieties"  
insert --(PM, SM or BASE)--.

Page 104, line 6, after "S, B and Sig" and before the comma ","  
insert --(PM, SM, BASE and Sig, respectively)--.

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Page 104, line 18, after the first word in the line "Sig" and before "and  
especially" insert the following  
--PM—SM—BASE—Sig --.

Page 105, line 8, after "Sig components" and before "wherein"  
insert --(PM, SM, BASE and Sig)--.

Page 105, line 10, after "moieties"  
insert --(PM, SM and BASE, respectively)--.

Page 105, line 23, after "P, S, B" insert --(PM, SM, BASE)--.

Page 105, line 15, after "Sig-containing"  
insert --(PM, SM, BASE and Sig, respectively)--.

Page 110, line 9, after "the sugar S" insert --(SM)--.

**In The Claims:**

Cancel claim 1.

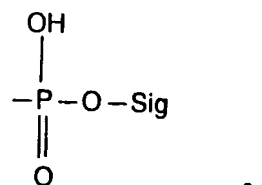
Add new claims 204-233 as follows:

-- 204. (NEW) A nucleotide having the formula

Sig - PM - SM - BASE

wherein PM is a phosphate moiety, SM is a sugar moiety and BASE is a pyrimidine, purine or 7-deazapurine moiety, PM being attached to the 3' or the 5' position of the sugar moiety when said nucleotide is a deoxyribonucleotide and at the 2', 3' or 5' position when said nucleotide is a ribonucleotide, BASE being attached to the 1' position of SM from the N<sup>1</sup> position when BASE is a pyrimidine or the N<sup>9</sup> position when BASE is a purine or 7-deazapurine, and Sig is covalently attached to PM directly or via a chemical linkage, said Sig being a detectable moiety when attached to PM. --

-- 205. (NEW) The nucleotide of claim 204 wherein said covalent linkage comprises



-- 206. (NEW) The nucleotide of claim 204 wherein said chemical linkage does not interfere substantially with the characteristic ability of Sig to form a detectable signal. --

-- 207. (NEW) The nucleotide of claim 204 wherein Sig is a moiety containing at least three carbon atoms. --

-- 208. (NEW) The nucleotide of claim 204 wherein Sig includes a glycosidic linkage moiety. --

-- 209. (NEW) The nucleotide of claim 204 wherein Sig comprises a component selected from the group consisting of biotin, iminobiotin, an electron dense component, a magnetic component, an enzyme, a hormone component, a radioactive component, a metal-containing component, a fluorescent component, a chemiluminescent component, an antigen, a hapten and an antibody component. --

-- 210. (NEW) The nucleotide of claim 209 wherein said electron dense component comprises ferritin. --

-- 211. (NEW) The nucleotide of claim 204 wherein Sig is complexed with a binding protein therefor, and said binding protein is conjugated to ferritin. --

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- 212. (NEW) The nucleotide of claim 209 wherein Sig comprises a magnetic component. --
- 213. (NEW) The nucleotide of claim 212 wherein said magnetic component comprises a magnetic oxide. --
- 214. (NEW) The nucleotide of claim 213 wherein said magnetic oxide is ferric oxide. --
- 215. (NEW) The nucleotide of claim 209 wherein Sig comprises an enzyme. --
- 216. (NEW) The nucleotide of claim 215 wherein said enzyme is selected from the group consisting of alkaline phosphatase, acid phosphatase,  $\beta$ -galactosidase, ribonuclease, glucose oxidase and peroxidase. --
- 217. (NEW) The nucleotide of claim 209 wherein Sig comprises a radioactive component. --
- 218. (NEW) The nucleotide of claim 217 wherein said radioactive component is radioactive cobalt. --
- 219. (NEW) The nucleotide of claim 209 wherein Sig comprises a metal-containing component. --
- 220. (NEW) The nucleotide of claim 219 wherein said metal-containing component is catalytic. --
- 221. (NEW) The nucleotide of claim 209 wherein Sig comprises a fluorescent component. --

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-- 222. (NEW) The nucleotide of claim 221 wherein said fluorescent component comprises a member selected from the group consisting of fluorescein, rhodamine and dansyl. --

-- 223. (NEW) The nucleotide of claim 209 wherein Sig comprises a chemiluminescent component. --

-- 224. (NEW) The nucleotide of claim 209 wherein Sig comprises a hapten component capable of complexing with an antibody specific thereto. --

-- 225. (NEW) An oligo- or polydeoxyribonucleotide comprising at least one nucleotide in accordance with claim 204. --

-- 226. (NEW) An oligo- or polyribonucleotide comprising at least one nucleotide in accordance with claim 204. --

-- 227. (NEW) An oligo- or polynucleotide comprising at least one nucleotide of claim 204 and wherein the oligo- or polynucleotide is terminally ligated or attached to a polypeptide. --

-- 228. (NEW) A composition comprising an oligo- or polynucleotide including at least one nucleotide of claim 204, a polypeptide capable of forming a complex with Sig and a moiety which can be detected when such complex is formed. --

-- 229. (NEW) The composition of claim 228 wherein said polypeptide comprises a polylysine. --

-- 230. (NEW) The composition of claim 228 wherein said polypeptide is selected from the group consisting of avidin, streptavidin and anti-Sig immunoglobulin. --

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-- 231. (NEW) The composition of claim 228 wherein Sig is a ligand  
and said polypeptide is an antibody thereto. --

-- 232. (NEW) The composition of claim 228 wherein said detectable  
moiety is selected from the group consisting of biotin, iminobiotin, an  
electron dense component, a magnetic component, an enzyme, a hormone  
component, a radioactive component, a metal-containing component, a  
fluorescent component, a chemiluminescent component, an antigen, a  
hapten and an antibody component. --

-- 233. (NEW) The nucleotide of claim 232 wherein said detectable  
moiety comprises a chemiluminescent component. --

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